

Award Number: W81XWH-15-1-0614

TITLE: Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury

PRINCIPAL INVESTIGATOR: Ona Bloom

CONTRACTING ORGANIZATION: The Feinstein Institute for Medical Research
Manhasset, NY 11030

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14. ABSTRACT Immediately after SCI, a person confronts 3 major questions: (1) how much function have they lost, (2) what treatments promote recovery, (3) how much physical recovery can they expect over time? To answer the first question, a clinical exam tests motor and sensory function throughout the body. The second question is still largely unanswered: standard rehabilitation focuses on maximizing preserved function and managing medical complications of living with SCI. Currently, there is no FDA-approved drug to promote recovery after SCI. The third question is also unanswered; there is no standardized model to predict functional recovery, which occurs mostly within the first year after SCI. Surprisingly little is known about the biological processes influencing recovery after SCI. Experiments indicate that inflammation worsens the initial area of damage and inhibits physical recovery. Signs of inflammation occur in people newly injured and in people living with SCI for many years. Our hypothesis is that some inflammatory factors are higher in individuals with SCI that achieve less physical recovery. We are performing a prospective, longitudinal study to measure circulating biochemical responses and functional recovery throughout the 1st year after SCI, within the same individuals. Data will be used to derive a predictive, multiscale model of functional recovery after SCI. The goal is to build an easy-to-implement, predictive model of functional recovery after SCI that incorporates biomarkers related to inflammation.					
15. SUBJECT TERMS traumatic spinal cord injury, spinal cord, spontaneous recovery, functional recovery, inflammation, biomarkers, trauma					
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1. **INTRODUCTION:** Immediately after a traumatic spinal cord injury (SCI), a person confronts 3 major questions: (1) how much function have they lost, (2) what treatments promote recovery, and (3) how much physical recovery can they expect over time? To answer the first question, a clinical exam tests motor and sensory function throughout the body. The second question is still largely unanswered: standard rehabilitation focuses on maximizing preserved function and managing medical complications of living with SCI. Currently, there is no FDA-approved drug to promote recovery after SCI. The third question is also unanswered; there is no standardized model to predict functional recovery, which occurs mostly within the first year after SCI. Surprisingly little is known about the biological processes influencing recovery after SCI. Experiments indicate that inflammation worsens the initial area of damage and inhibits physical recovery. Signs of inflammation occur in people newly injured and in people living with SCI for many years. Our hypothesis is that some inflammatory factors are higher in individuals with SCI that achieve less physical recovery. To test this hypothesis, we are performing a multi-site prospective, longitudinal study to measure circulating biochemical responses and functional recovery throughout the 1st year after SCI, within the same individuals. Data will be collected at least once within 0-3 days post injury (dpi), and then at 3, 6, and 12 months after SCI. The goal is to use these data to build an easy-to-implement, predictive multi-scale model of functional recovery after SCI that incorporates biomarkers related to inflammation.

2. **KEYWORDS:**

traumatic spinal cord injury, spinal cord, inflammation, biomarkers, spontaneous recovery, functional recovery, trauma

3. **ACCOMPLISHMENTS:**

▪ **What were the major goals of the project?**

Site 1: The Feinstein Institute for Medical Research (of Northwell Health), Site 2: Kessler Foundation, Site 3: University (Univ.) of Louisville. The major goals, as stated in the Statement of Work (SOW), are described below.

Major Task 1: Obtain IRB and HRPO/ACURO permission for study (Status: ongoing)

Timeline: months 1-9, October 2015-June 2016, due date 6/30/2016

Subtask 1: Submit documents for local IRB review: 100% completed.

Subtask 2: Submit IRB approval and necessary documents for HRPO review: 66% completed

- Site 1: initial approval obtained 2015-10-28, follow up approval received 2015-11-23, amendment approval 2016-09-07. Continuing renewal due to HRPO 2016-11-17.
- Site 2: Kessler was delayed in obtaining IRB permission, which was achieved just after the conclusion of Year 1.
- Site 3: initial approval received 2015-12-23, Continuing renewal approval 2016-09-07.

Major Task 2: Create Infrastructure and Obtain All Supplies/Training for Performance of Outcome Measures (Status: Completed)

Timeline: months 1-6, October 2015-March 2016, Q1-Q2 Yr 1, due date 3/31/2016

Subtask 1: Instruction or Review of Functional Outcome measures. Months 1-6, October 2015-March 2016, Q1-Q2, Yr 1, due date 3/31/2016. Status: 100% complete.

- Site 1 Physical therapists who are study personnel attended the NeuroRecovery Training Institute 2-day training course March 4-6, 2016 at The Kessler Institute (NJ).
- Site 1 review of SCIM scoring criteria was held locally on April 12, 2016.

Subtask 2: non-NRN site personnel visit NRN site(s) for observational case study learning.

Months 1-6, October 2015-March 2016, Q1-Q2, Yr 1, due date 3/31/2016. Status: ongoing

- Site 1: The Introductory NRN training course was augmented by physical therapists who are study personnel with an NRTI online course (*Adult Neuromuscular Recovery Scale: A New Outcome Measure for Spinal Cord Injury Based on Pre-injury Function*) in the NeuroRecovery Scale (NRS), a relatively new functional outcome measure used in this study. Subsequently, NRS is now being used in clinical practice by some Site 1 study personnel, where appropriate, thereby providing local case study learning.

Subtask 3: Create custom clinical database for data entry: 100% completed.

- Personnel at Site 1 created a HIPAA-compliant custom internet accessible study database for use by all sites. This site was then tested by study personnel from all 3 sites and refined based on feedback prior to going live.

Subtask 4: Create SOP for clinical team, including data entry forms and instruction on use: 100% completed.

- Case report forms (CRF) were created with input from study personnel at all sites.
- Standard Operating Protocol (SOP) was created with input from study personnel at all sites.
- Instructions on use of CRF were created at Site 1 and then refined after testing by personnel at all sites.
- Study personnel at sites 2 and 3 were instructed by study personnel at Site 1 on use of CRF, SOP, and data entry into study database.

Subtask 5: Send sample collection supplies, SOP and shipping supplies to all sites: 100% completed.

- Site 1 sent supplies to all sites and continues to do so as needed.

Major Task 3: Human Subject Study Enrollment (Status: Ongoing)

Timeline: months 7-30, April 2016-March 2018, Q3 Yr 1-Q2 Yr 3, due date 3/31/2018

Subtask 1: Recruit, consent and enroll subjects at acute time points (study visit 1).

Site 1 Feinstein: The research coordinator and/or the PI meets daily with clinical study personnel to screen potential participants. Within Year 1, 19 patients with spinal cord injury were screened. Of them, 4 participants enrolled, 1 declined to enroll, 14 did not meet study eligibility criteria.

Site 3 Kentucky: Within year 1, 10 patients with spinal cord injury were screened. Of them, 1 participant enrolled, 5 declined to enroll, 4 did not meet study eligibility criteria.

Subtask 2: Obtain Biological Samples (blood) from subjects, study visits 1-4:

Site 1: Biological samples were collected from 4 participants at study visit 1.

Site 3: Biological samples were collected from 1 participant at study visit 1.

Subtask 3: Process and store biological samples:

Site 1: Samples were processed and stored from 4 participants at study visit 1.

Site 3: Samples were processed, shipped to Site 1 and stored from 1 participant at study visit 1.

Subtask 4: Perform ISNCSCI exams and determine AIS grades:

Sites 1 and 3: Exams were performed for potential participants as necessary/medically possible during the screening process and for all enrolled participants.

- **What was accomplished under these goals?**

1) Major Activities:

Major activities were focused on completing SOW Major Tasks 1-3: obtaining permission from regulatory bodies to initiate the project, creating the infrastructure to do so, obtaining supplies and training to perform all outcome measures, initiation of participant enrollment. We also established and are maintaining regular communication between all sites via a monthly conference call between all sites to discuss study progress and to optimize maintenance of SOW goals. This was held 10 times during Year 1.

2) Specific Objectives of the Project:

- Major Task 1 was to obtain IRB and HRPO/ACURO permission for study. This was accomplished at Sites 1 and 3. (As mentioned above, IRB approval has now been achieved at Site 2.)
- Major Task 2 was to create the infrastructure and obtain all supplies and training needed to perform all outcome measures. This was accomplished.

- Major Task 3 was to initiate human subject study enrollment. This was accomplished at Sites 1 and 3, where a combined total of 29 participants were screened and 5 were enrolled in the study.

3) *Significant or key outcomes: major findings, developments or conclusions:*

As we are concluding Year 1 of a study that requires human subject research, we have not yet generated major findings or drawn major conclusions from the study.

4) *Other achievements:*

What opportunities for training and professional development has the project provided?

Training:

Site 1:

- Feinstein is the non-NeuroRecovery Network (NRN) site participating in this study. As stated above, physical therapists that are study personnel attended the NeuroRecovery Training Institute (NRTI) 2-day training course held at The Kessler Institute for Rehabilitation (Site 2). Training was later augmented by completion of an NRTI online course, “*Adult Neuromuscular Recovery Scale: A New Outcome Measure for Spinal Cord Injury Based on Pre-injury Function*,” a functional outcome measure used in this study. NRS is now being used in clinical practice by some study personnel, where appropriate, thereby providing local case study learning and broadening the impact of the study.
- At Site 1, review of the scoring criteria for the Spinal Cord Independence Measure (SCIM) was also held for relevant study personnel.

Site 2:

- The NRTI training course attended by Site 1 was held at Site 2. Dr. Forrest, Site 2 PI, participated in the training course.

Professional Development:

Site 1:

- To enhance her professional development in support of this study, Ms. Rachel Monahan, Research Coordinator (Site 1) attended an on-site course “*Preparing for Certification as a Clinical Research Coordinator*”.
- Dr. Bloom attended several professional conferences to present other SCI related work ongoing in her lab and to learn about other efforts ongoing and topics of interest in SCI research. (Travel to these meetings was not funded by the DOD.):
 - October, 2015 Annual meeting of the Society for Neuroscience (SFN)
 - December, 2015 International Symposium on Neural Regeneration (ISNR)
 - April, 2016 Annual meeting of the American Spinal Injury Association (ASIA)

How were the results disseminated to communities of interest?

Although we do not yet have results from this study, Dr. Bloom (PI) presented the scientific background, study design and goals at 2 external seminars/conferences:

- Grand Rounds, Northport Stony Brook VA Medical Center, Northport, NY. August, 2016
- International Symposium on the Neurobiology of Locomotion (in honor of Dr. Avis Cohen, Univ. of Maryland), George Washington University, Washington, DC. June, 2016

Dr. Bloom (PI) also presented the scientific background, study design and goals at 2 internal seminars:

- Grand Rounds, Department of Physical Medicine and Rehabilitation Grand Rounds, Hofstra Northwell School of Medicine, Hempstead, NY. 2016.
- Grand Rounds, Department of Neurosurgery Grand Rounds, Lenox Hill Hospital, NY, NY. 2016

▪ **What do you plan to do during the next reporting period to accomplish the goals?**

We will follow the scheduled list of tasks stated on the Statement of Work:

- Major Task 3: Human Subject Study Enrollment.
 - Subtask 1: Recruit, consent and enroll subjects at acute time points (study visit 1).
 - Subtask 2: Obtain Biological Samples (blood) from subjects, study visits 1-4
 - Subtask 3: Process and store biological samples, study visits 1-4

Subtask 4: Perform ISNCSCI exams and determine AIS grades, study visits 1-4

Subtask 5: Administer SCIM and determine scores, study visits 2-4, with support personnel as indicated in budget justifications

Subtask 6: Administer NRS and determine scores, study visits 2-4, with support personnel as indicated in budget justifications

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?**
Nothing to report.
- **What was the impact on other disciplines?** Nothing to report.
- **What was the impact on technology transfer?** Nothing to report.
- **What was the impact on society beyond science and technology?** Nothing to report.

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**
 - We have not had significant changes in the approach of the project.
- **Actual or anticipated problems or delays and actions or plans to resolve them**

Site 1: Site 1 enrolled 4 participants during Year 1, slightly ahead of the recruitment schedule stated on the SOW. Unfortunately, all of these participants declined to continue study participation when contacted to arrange their 3-month study visit. This is typically a challenging time for persons with SCI, who are either in the initial phases of adjusting to living with SCI at home or may still be at a rehabilitation facility. In consultation with the site PIs and key personnel at all sites, Site 1 will request IRB (and then HRPO) permission for the following changes at their site, aimed to enhance participant retention:

1. Offer to conduct study visits at home (as well as in an institutional setting, as currently offered): A study personnel team may visit participants at home to perform the ISNCSCI exam (primary functional outcome measure), SCIM evaluation and obtain the biological samples. While it is not possible to perform the NRS evaluation in a home environment, we hope that offering to do study visits at home will encourage study participants to remain in the study, particularly at the 3 month follow up.
2. Establish better ongoing communication with study participants: A member of the study team will reach out to study participants by phone on a regular (e.g. monthly) basis in order to maintain contact and build a rapport.
3. Assist in travel arrangements to study visits: We will offer to arrange for and pay for ambulette service to the closest study site. Travel is not a trivial issue for many people with SCI and we hope that offering additional support will enable participants to attend 3, 6 and 12 month study visits.

Site 2: There was a delay at Kessler (Site 2) in obtaining IRB permission to initiate the study. This is partly due to the effects of the New Jersey Medical and Health Sciences Education Restructuring Act, which recently designated University Hospital in Newark as an independent institution. As University Hospital is the site of initial participant recruitment for Site 2, the changes in governance have made the IRB process unexpectedly lengthy and complex. Initial local IRB approval at Kessler was obtained on 10/21/2015 and revised approval obtained on 12/14/2015. This protocol was submitted to the IRB at Rutgers University on 3/2/2016. As of 10/6/2016, this protocol was approved. Kessler will submit the documentation to HRPO and we are expecting to initiate the study at Site 2 shortly thereafter.

- **Changes that had a significant impact on expenditures**

Although participant retention was a challenge at Site 1, recruitment was ahead of schedule, so this has not significantly altered expenditures. As Site 2 (Kessler) has not yet initiated study screening and enrollment, this delayed expenditures at their site.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents-**Not applicable.
- **Significant changes in use or care of human subjects -**Not applicable.
- **Significant changes in use or care of vertebrate animals-**Not applicable.
- **Significant changes in use of biohazards and/or select agents-**Not applicable.
-

6. PRODUCTS:

- **Publications, conference papers, and presentations.**
- **Journal publications.** Nothing to Report
- **Books or other non-periodical, one-time publications.** Nothing to Report
- **Other publications, conference papers, and presentations.**
As stated above, Dr. Bloom (PI) presented the scientific background, study design and goals at 2 external and 2 internal seminars/conferences:
 - Grand Rounds, Northport Stony Brook VA Medical Center, Northport, NY. August, 2016
 - International Symposium on the Neurobiology of Locomotion (in honor of Dr. Avis Cohen, Univ. of Maryland), George Washington University, Washington, DC. June, 2016
 - Grand Rounds, Department of Physical Medicine and Rehabilitation Grand Rounds, Hofstra Northwell School of Medicine, Hempstead, NY. 2016.
 - Grand Rounds, Department of Neurosurgery Grand Rounds, Lenox Hill Hospital, NY, NY. 2016
- **Website(s) or other Internet site(s):** This study is listed on clinicaltrials.gov:
<https://clinicaltrials.gov/ct2/show/NCT02731027?term=biomarkers+of+spinal+cord+injury&rank=2>
- **Technologies or techniques-**Not applicable.
- **Inventions, patent applications, and/or licenses-** Not applicable.
- **Other Products-**Not applicable.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

▪ What individuals have worked on the project?

What Individuals have worked on the project? ≥ 1 person month this year	Site 1: Feinstein Institute for Medical Research
Name:	Ona Bloom, PhD
Project Role:	Overall PI
Researcher Identifier (e.g. ORCID ID):	0000-0002-8340-2392
Nearest person month worked:	3
Contribution to Project:	Dr. Bloom is responsible for overseeing all aspects of the project, supervises and participates in all on-site tasks and Site 1 personnel, and coordinates between study sites.
Funding Support:	DOD (3 calendar months), NY State Spinal Cord Injury Research Board, institutional support
Name:	Matthew Bank, MD
Project Role:	Co-investigator, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to	

Project:	
Funding Support:	
Name:	Adam Stein, MD
Project Role:	Co-investigator, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project	
Funding Support:	
Name:	Martin Lesser, PhD
Project Role:	Director, Biostatistics Unit, Site 1, (No Change from original submission)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project:	
Funding Support:	
Name:	James Tsang
Project Role:	Biostatistics Support
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1.2
Contribution to Project:	Supervised by Dr. Lesser, created and is maintaining the custom clinical database, developed plans for data monitoring, data management and reporting
Funding Support:	DOD (this grant). He is also supported by NIH grants and departmental funding for work on other projects.
Name:	Rachel Monahan
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	9
Contribution to Project:	Ms. Monahan submitted and maintained local IRB regulatory binder and correspondence, maintained all HRPO/ACURO related documents and correspondence, participated in development of case report forms, input data to clinical database, performed sample processing, biochemical assays shipped supplies to other sites, coordinated communication with other sites (monthly conference calls), trained other site personnel on how to use database for submitting data and participated in data analysis.

Funding Support:	DOD (this grant). She was also supported by institutional funds for her work supporting this and other projects.
What Individuals have worked on the project? ≥ 1 person month this year	Site 2: Kessler Foundation
Name:	Gail Forrest, PhD
Project Role:	Site 2 (Kessler) PI (No change from original submission.)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1.2
Contribution to Project	
Funding Support:	
Name:	LeighAnn Martinez
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2.4
Contribution to Project:	Ms. Martinez submitted and maintained local IRB regulatory binder and correspondence and related documents, participates in monthly study personnel conference calls
Funding Support:	DOD (this project). For other projects, she is supported by: NJCSCR, NIH, NIDILRR.
What Individuals have worked on the project? ≥ 1 person month this year	Site 3: University of Louisville
Name:	Max Boakye, MD (No Change from original submission)
Project Role:	Site 3 (Univ. of Louisville) PI (No change from original submission.)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	
Contribution to Project:	
Funding Support:	
Name:	Debra Williams
Project Role:	Research Coordinator (No change from original submission.)
Researcher Identifier (e.g. ORCID ID):	
Nearest person month	

worked:	
Contribution to Project:	
Funding Support:	
Name:	Yukishia Austin (No Change from original submission)
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	
Funding Support:	
Name:	Kelly Neese
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Neese participated in screening participants, research coordination, collecting data for case report forms and submitting them to custom database, participates in monthly study personnel conference calls
Funding Support:	DOD (this grant). She was also supported by NIH grants and departmental funding for work on other projects.
Name:	Neesha Settipalle
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Settipalle participated in screening participants, research coordination, collecting data for case report forms and submitting them to custom database, participates in monthly study personnel conference calls
Funding Support:	DOD (this grant). She was also supported by departmental funding for work on other projects.
Name:	Lori Clark
Project Role:	Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Ms. Clark participates in screening participants, research coordination, collecting data for case report forms and submitting them to custom

	database, participates in monthly study personnel conference calls
Funding Support	DOD (this grant). She is also supported by NIH grants and departmental funding for work on other projects.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Note: For all personnel listed below, the information provided is in addition to this DOD grant “*Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury*”.

Site 1: Feinstein Institute for Medical Research

Ona Bloom PhD, Principal Investigator (Feinstein Institute):

New Active Support:

National Institutes of Health (NIH) 1R01AR069668-01 Chahine (PI) 09/5/2016-08/31/2021

Mechanobiology of Inflammation in the Intervertebral Disc.

This is a grant to discover how inflammation affects different mechanical properties of intervertebral disc cells and contributes to disc degeneration.

Role: Co-Investigator, 1.2 Calendar Months, (10%).

New Active and now Completed Support:

NY State Spinal Cord Injury Research Board (NYSCIRB) DOH01-ISSCI5-2015-00016 Bloom (PI) 02/01/16-8/31/16
Biomarkers of Spontaneous Recovery from Traumatic Spinal Cord Injury.

During Year 1, NYSCIRB announced availability of short-term, non-renewable funding to NY State PIs who had at least 1 federally funded SCI research project, to expand aims or efforts towards the project. Support was used only at Site 1 to add a non-overlapping aims (flow cytometry of circulating leukocytes and additional biological samples during acute hospitalization beyond those supported by DOD), to enhance the information gained and hence the study's impact. Of course, the DOD will be acknowledged in any presentations or publications where this data is presented.

Role: Principal Investigator, 3 Calendar Months, (25%)

Martin Lesser PhD, Key Personnel

New Completed Support

NIH U34 AR063407 Mackay (PI) 09/25/13 – 08/31/16

Treatment of SLE with Ajulemic Acid, a Non-Psychoactive Cannabinoid Derivative.

The goal is evaluate the safety of ajulemic acid (AjA) in SLE patients with mild to moderate musculoskeletal pain and to determine an optimum dose of AjA to provide maximum benefit and minimal toxicity.

Role: Director, Biostatistics Unit, 0.18 Calendar Months (1.5%)

NINDS P50 NS071675-03 Eidelberg (PI) 09/01/10 – 08/31/16,

Morris K. Udall Center of Excellence for Parkinson's Disease. The goal of the Udall Center program is to utilize a multidisciplinary research approach to elucidate the fundamental causes of PD as well as to improve the diagnosis and treatment of patients with Parkinson's and related neurodegenerative disorders.

Role: Project Leader – Core Leader Statistical and Data Management, 1.0 calendar months (8%)

NINH R21 AR063929 Diamond (PI) 07/01/13 – 06/30/16

Nelfinavir SLE: A Pilot Phase IIa Clinical Trial, This is a study of the ability of nelfinavir to block DNA binding.

Role: Statistician, 0.6 Calendar Months, (5%)

NIDCD 1U01 DC007946-05 Steinberg (PI) 07/01/07 – 06/30/16

Celecoxib Therapy for Patient With Recurrent Respiratory Papillomatosis

The goal is to determine the efficacy of celecoxib therapy as an adjunct to surgery for RRP. Secondary aims address the effect of patient demographics & molecular markers of COX-2 inhibition on response.

Role: Statistician, 1.48 Calendar Months, (12%)

NIH/NIDCD, R21/R33 DC011827 Vambutas (PI) 07/01/11 – 06/30/15

An Open-Label Phase I Clinical Trial of Anakinra in Corticosteroid Resistant Patients with AIED The goal is to determine if Anakinra is able to restore hearing and corticosteroid resistant patients with AIED.

Role: Statistician

NIH 1 R21CA178864-04 McDonald (PI) 09/20/13 – 09/31/15

MicroRNAs and Early Prostate Cancer Detection. Goal: To reduce prostate cancer incidence and mortality in high-risk populations by identifying microRNAs which will better screen for prostate cancer.

Role: Statistician, 0.24 Calendar Months (2%)

NCI 5U10 CA35279 Vinciguerra (PI) 06/01/10 – 05/31/15

North Shore University Hospital CCOP, Goal: This is a community oncology program to promote research protocol treatment of cancer patients.

Role: Statistician

Peter Gregersen MD, Key Personnel:

New Active Support

NIH R21AR067012-01A1 Diamond (PI) 06/01/15-05/31/17

Function of the IRF5 risk allele for SLE in B cells This is a study of the functionality of the IRF5 risk allele in B cells of healthy individuals.

Role: Co-investigator, 0.2 Calendar Months, (1.7%)

NIH 1UG30D023391-01 Gregersen (PI) 09/21/16-08/31/18

ECHO – Environmental Influences on Childhood Health Outcomes - Prenatal Autoimmune and Inflammatory Risk Factors for Autism Spectrum Disorders

This project focuses on the role of *in utero* exposure to maternal autoimmunity in determining neurodevelopmental outcomes of the offspring.

Role: Co-investigator, 1.2 Calendar Months, (10%)

New Completed Support

Biogen/IDEC Gregersen (PI) 6/1/10-5/31/15 *Biomarkers of Anti-TNF- α Therapy Efficacy in Rheumatoid Arthritis to Define Unresponsive Patients (BATTER-UP)*

The goal of this study is to develop a way to predict which patients with rheumatoid arthritis will benefit from anti-TNF therapy.

Role: Principal Investigator, 0.6 Calendar Months, (5%)

NIH 5R21AR065199-02 Gregersen (PI), Diamond, B (Co-PI) 7/1/13-6/30/15

Genetic and functional investigations of human TNIP1 haplotypes associated with Systemic Lupus Erythematosus, Systemic Sclerosis and Early Onset Myasthenia Gravis.

Role: Co-Principal Investigator, 1.2 Calendar Months, (10%)

NIOSH 1U01-OH010512-01A1 Taioli (PI) 07/01/14-06/30/16

Biorepository of Cancer Tissue Samples from WTC Responders

The current project aims to establish a biorepository of cancer tissue samples from World Trade Center (WTC) Responders. This biorepository will consolidate tissue samples from all those in the WTC cohort that consent to participate. These samples will be stored in a centralized location, de-identified, and catalogued. This will allow for future research into WTC-specific mechanisms involved in cancer development, and will result in improved treatment options for WTC responders.

Role: Co-Investigator, 0.6 Calendar Months, (5%)

Mathew Bank MD, Co-Investigator (3 calendar months): Nothing to Report

Adam Stein MD, Co-Investigator (0.6 calendar months): Nothing to Report

Site 2: Kessler Foundation

Gail Forrest PhD, Site PI (Kessler):

New Active Support:

NIH 1R21NS095052 Jiang (PI) 4/1/16 – 3/31/18

Longitudinal Assessment of Spinal Cord Structural Plasticity using DTI in SCI Patients. This study will apply novel magnetic resonance imaging (MRI) techniques to investigation of spinal cord injury (SCI) to learn how nerve fibers repair and neural cells regain ability to control muscle during the rehabilitation. The information gained will be helpful for physicians to make more accurate diagnosis of SCI, predict injury recovery and movement restoration, and develop more effective treatment plans.

Role: Co-Investigator, 0.60 Calendar Months (5%)

NIDILRR 90RE5021 Foulds (PI) 9/30/15 – 9/29/21

Rehabilitation Engineering Research Center on Wearable Robots for Independent Living, Subrecipient Agreement From New Jersey Institute of Technology (NJIT). This project conducts research and development activities focused on wearable robots for independent mobility and manipulation. This RERC is a joint effort of the NJIT and the Kessler Research Foundation comprising three research and two comprehensive development projects, plus a portfolio of training activities. Two of the research projects employ three commercially available, lower extremity exoskeletons.

Role: Co-Investigator, 0.60 Calendar Months (5%)

EMD Serono PI: Sandroff (PI) 7/15/16 – 7/14/19

Effects of Walking Exercise Training on Learning and Memory Outcomes in MS, Impairment of learning and memory, namely impairment in learning new information, is highly prevalent, disabling, and poorly-managed in MS. Exercise training represents a promising behavioral approach for managing this consequence of the disease. This line of research proposes the development of exercise training guidelines that can be adapted by clinicians for use by MS patients for specifically improving cognition and brain health.

Role: Co-Investigator, 0.72 Calendar Months (6%)

New Completed Support:

Parker Hannifin, Forrest (PI) 5/5/14-7/7/2015

A Multi-Center, Interventional Study to Evaluate the Efficacy and Safety of the Indego Robotic Exoskeleton Device in Subjects with Lower Extremity Weakness or Paralysis. The major goals of this project are to train 10 individuals with SCI using the Indego exoskeleton and collect data on safety and efficacy for an FDA submission. In addition health related data will also be collected at set time points during the trial.

Role: Site Principal Investigator, 1.2 Calendar Months (10%)

Craig H. Neilsen Foundation, 191152, Forrest (PI) *Activity-Dependent Rehabilitation Model to Improve Bone and Muscle after SCI*, 7/1/14-12/31/15. The major goals of this project are to measure the changes in muscle and bone after multi muscle neuromuscular electrical stimulation (NMES) and stand training compared to NMES alone and stand alone for chronic complete SCI.

Role: Principal Investigator, 0.12 Calendar Months (1%)

Steven Kirshblum, MD (Key Personnel, Kessler)

New Active Support:

Craig H. Neilsen Foundation, 360924, O'Neill (PI) 12/31/15 – 12/31/18.

Resource Facilitation: Early Inpatient and Assertive Outpatient VR Services for Individuals with SCI, This project will deliver vocational services to individuals with spinal cord injury (SCI) starting during the inpatient stay followed by systematic and assertive employment service coordination post discharge for two years leading to competitive employment.

Role: Collaborator, 0.12 Calendar Months (1%)

NIH 1R21NS095052, Jiang (PI) *Longitudinal Assessment of Spinal Cord Structural Plasticity using DTI in SCI Patients*, 4/1/16 – 3/31/18 This study will apply novel magnetic resonance imaging (MRI) techniques to investigation of spinal cord injury (SCI) to learn how nerve fibers repair and neural cells regain ability to control

muscle during the rehabilitation. The information gained will be helpful for physicians to make more accurate diagnosis of SCI, predict injury recovery and movement restoration, and develop more effective treatment plans.

Role: Co-Investigator, 0.24 Calendar Months (2%)

NIDILRR 90RE5021 Foulds (PI) *Rehabilitation Engineering Research Center on Wearable Robots for Independent Living*, 9/30/15 – 9/29/21, Subrecipient Agreement From New Jersey Institute of Technology (NJIT). This project conducts research and development activities focused on wearable robots for independent mobility and manipulation. This RERC is a joint effort of the NJIT and the Kessler Research Foundation comprising three research and two comprehensive development projects, plus a portfolio of training activities. Two of the research projects employ three commercially available, lower extremity exoskeletons.

Role: Co-Investigator, 0.12 Calendar Months (1%)

New Completed Support:

Craig H. Neilsen Foundation, 191152, Forrest (PI) Activity-Dependent Rehabilitation Model to Improve Bone and Muscle after SCI, 7/1/14-12/31/15. The major goals of this project are to measure the changes in muscle and bone after multi muscle neuromuscular electrical stimulation (NMES) and stand training compared to NMES alone and stand alone for chronic complete SCI.

Role: Co-Investigator, 0.12 Calendar Months (1%)

Site 3: University of Louisville

Max Boakye, MD Site PI (University of Louisville):

New Active Support:

Helmsley Charitable Trust Harkema (PI) 12/15/15–12/14/19

Helmsley Center for Restorative Medicine

The goal of this project is to define the temporal profile of cardiac, pulmonary, vascular, and metabolic dysfunction after SCI and develop novel therapeutic approaches to treat those conditions.

Role: Co-Investigator, 11%

Helmsley Charitable Trust Harkema (PI) 07/15/15-06/30/18

Recovery of Function, Health and Quality of Life for People with Paralysis

The major goal is to restore motor function and quality of life in patients with spinal cord injury using epidural stimulation and locomotor training therapies.

Role: Co-Investigator, 1.8 Calendar Months (15%)

Paralyzed Veterans of America Research Foundation #3010 Boakye (PI) 01/01/15-12/31/16

Improving acute SCI assessment with Cine MRI and epidural electrophysiology

The major goal of this project is to use advanced MRI and intraoperative epidural electro-physiological techniques to improve assessment of acute SCI during the critical period when the cord is at greatest risk for secondary injury.

Role: PI, 1.8 Calendar Months (15%)

New Completed Support:

KSCHIRT #11-7 Harkema (PI) 02/01/12-01/31/15

Neurophysiological assessment of residual supraspinal input after human spinal cord injury

The major goal is to restore motor function and quality of life in patients with spinal cord injury using epidural stimulation and locomotor training therapies.

Role: Co-Investigator, 1.8 Calendar Months (15%)

Susan Harkema, PhD Co-Investigator (Louisville):

New Active Support:

Helmsley Charitable Trust Harkema (PI) 12/15/15–12/14/19

Helmsley Center for Restorative Medicine The goal of this project is to define the temporal profile of cardiac, pulmonary, vascular, and metabolic dysfunction after SCI and develop novel therapeutic approaches to treat those conditions.

Role: Principal Investigator, 2.4 Calendar Months (20%)

CTN10 Harkema (PI) 06/01/12-05/31/17

DOD/Christopher & Dana Reeve Foundation *North American Clinical Trials Network (NACTN)* The major goal of this project is to achieve clinical trials capable of indicating effectiveness of promoting spinal cord injury (SCI) therapies.

Role: Principal Investigator, 0.36 Calendar Months (3%)

Helmsley Charitable Trust Harkema (PI) 07/15/15-06/30/18

Recovery of Function, Health and Quality of Life for People with Paralysis

The major goal is to restore motor function and quality of life in patients with spinal cord injury using epidural stimulation and locomotor training therapies.

Role: Principal Investigator, 2.4 Calendar Months (20%)

New Completed Support:

NIDRR H133N110007 Graves (PI) 10/01/11-9/30/16

Spinal Cord Injury Model System (SCIMS). The major goal of this project is to establish a Model System of spinal cord medicine to provide integrated multidisciplinary system of rehabilitation care specifically designed to meet the needs of individuals with SCI.

Role: Co-Investigator, 1.2 Calendar Months (10%)

260957 Marino (PI) 07/1/13-6/30/16

Craig H. Neilsen Foundation/Thomas Jefferson University

Responsiveness of the Capabilities of Upper Extremity Test (CUE-T)

The major goal of this research is to determine the responsiveness of the Capabilities of Upper Extremity Test (CUE-T), a comprehensive, objective assessment of upper extremity functional capabilities in persons with cervical spinal cord injury (SCI), in order to determine whether it could be used as an outcome measure for clinical trials and treatment interventions

Role: Collaborator, 0.192 Calendar Months (1.6%)

Kessler Foundation, Inc., 357-01, Forrest (PI) 01/1/11-12/31/2015

An activity-dependent rehabilitation model to improve bone and muscle for sub acute to chronic SCI. The major goal of this project is to examine the effectiveness of stand training with electrical stimulation to induce positive changes in bone.

Role: Co-Investigator, 0.12 Calendar Months (1%)

KSCHIRT #11-7 Harkema (PI) 02/01/12-01/31/15

Neurophysiological assessment of residual supraspinal input after human spinal cord injury.

The major goal is to restore motor function and quality of life in patients with spinal cord injury using epidural stimulation and locomotor training therapies.

Role: Co-Investigator, 1.8 Calendar Months (15%)

National Institute of Health (NIBIB) R01 EB007615 Edgerton (PI) 09/1/08-8/31/14

Spinal epidural electrode array to facilitate standing and stepping after SCI.

The major goal of this research is to investigate the combined effects of stand and step (locomotor) training with electrical stimulation of the spinal cord in individuals who have had a complete SCI.

Role: Co-Investigator

ES1-2010 Christopher & Dana Reeve Foundation Harkema (PI) 04/01/11-3/31/13

Epidural Stimulation Project Facilitation of Standing and Stepping following SCI with Epidural Stimulation.

The major goal of this research is to investigate the combined effects of stand and step (locomotor) training with electrical stimulation of the spinal cord in individuals who have had a complete SCI.

Role: Principal Investigator

▪ **What other organizations were involved as partners?**

There are 3 academic institutions collaborating in this study.

Organization 1 Name: Feinstein Institute for Medical Research (of Northwell Health)

Location of Organization: Manhasset, NY

Partner's contribution to the project (*identify one or more*)

Financial support; Some institutional salary support is provided for the PI and additional study personnel.

In-kind support (*e.g., partner makes software, computers, equipment, etc., available to project staff*) Computers and equipment are available to project staff as needed.

Facilities (*e.g., project staff use the partner's facilities for project activities*): Facilities are available for the project staff.

Collaboration (*e.g., partner's staff work with project staff on the project*): This is the site of the overall PI. We have participated in all aspects of study design and tasks included in Major Tasks 1-3.

Organization 2 Name: The Kessler Foundation

Location of Organization: *West Orange, NJ*

Partner's contribution to the project (*identify one or more*)

Financial support:

In-kind support (*e.g., partner makes software, computers, equipment, etc., available to project staff*); Computers and equipment are available to project staff as needed.

Facilities (*e.g., project staff use the partner's facilities for project activities*): Facilities are available for the project staff.

Collaboration (*e.g., partner's staff work with project staff on the project*): Personnel have participated in all aspects of study design and Major Task 1-2. They are hoping to begin Major Task 3 immediately.

Organization 3 Name: University of Louisville

Location of Organization: *Louisville, KY*

Partner's contribution to the project (*identify one or more*)

Financial support:

In-kind support (*e.g., partner makes software, computers, equipment, etc., available to project staff*); Computers and equipment are available to project staff as needed.

Facilities (*e.g., project staff use the partner's facilities for project activities*): Facilities are available for the project staff.

Collaboration (*e.g., partner's staff work with project staff on the project*): Personnel are collaborating on the project. They have participated in all aspects of study design and tasks included in Major Tasks 1-3. This site is actively screening and enrolling participants.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *NOT APPLICABLE-THIS IS A SINGLE PI AWARD.*

QUAD CHARTS: Please see attached.

9. APPENDICES: None.

ADDITIONAL NOTES:

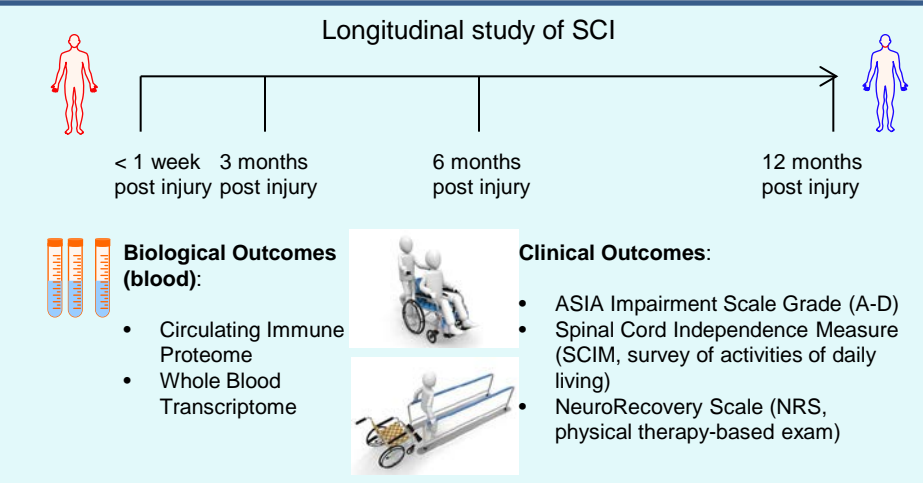
MARKING OF PROPRIETARY INFORMATION: Not applicable.

Study Aims

- 1. Identify the circulating inflammatory response for each SCI subject.
- 2. Determine the trajectory of spontaneous functional recovery for each traumatic spinal cord injury (SCI) subject.
- 3. Derive a predictive, multiscale model of functional recovery after SCI.

Approach

In order to improve classification and prognosis for people with traumatic SCI, we will conduct an observational, prospective, longitudinal, multi-site study of individuals with traumatic SCI during the 1st year post SCI, when most spontaneous recovery is achieved. At each study visit, we will measure biological responses (from sera) and functional recovery.



Accomplishments: Major Tasks 1-3 were achieved at 2 of 3 sites.

Progress on the task

Timeline and Cost

Major Tasks	CY	15	16	17	18
1. Obtain IRB/HRPO permission for study					
2. Create study infrastructure, complete training					
3. Human Subject Study Enrollment					
4. Data Analysis, Modeling & Interpretation					
Estimated Budget (\$K)		\$124,884	\$374,652	\$582,625	\$594,734

Updated: 10/19/2016

Goals/Milestones

- CY15 Goal –**
- Major Task 1: Obtain IRB/HRPO permission to initiate study: 66% complete (2/3 sites). (*Now completed, after Year 1 reporting date.)
- CY16 Goal-**
- Major Task 2: Create Infrastructure, obtain supplies/training for performance of outcome measures
- Milestone #1: HRPO approval at 2/3 sites. To be completed shortly.*
 - Milestone #2: Infrastructure & tools obtained to begin enrollment
- Major Task 3: Human Subject Study Enrollment
- Subtasks 1-4: Recruit, Biological Sample Collection, perform ISNCSCI exams, study visits 1-4: Efforts ongoing at Sites 1&3, initiating at Site 2.
 - Subtasks 5-6: Administer SCIM and NRS, study visits 2-4: Scheduled to be done as appropriate for enrolled participants.

Budget Expenditure to Date:
Projected Expenditure: \$499,536 Actual Expenditure: \$340, 950